

Philippine COVID-19 Living Clinical Practice Guidelines

Institute of Clinical Epidemiology, National Institutes of Health, UP Manila In cooperation with the Philippine Society for Microbiology and Infectious Diseases Funded by the DOH AHEAD Program through the PCHRD

CLINICAL RISK ASSESSMENT FOR SURGERY

RECOMMENDATIONS

We recommend using both clinical risk assessment and RT-PCR* to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery. (Very low quality of evidence; Strong recommendation)

We recommend using both clinical risk assessment and Antigen-Rapid Diagnostic Test (Ag-RDT)** to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery when RT-PCR testing is not available or when prolonged turnaround time is a concern. (Very low quality of evidence; Strong recommendation)

*Always use high-risk PPE regardless of RT-PCR or Ag-RDT test results in areas with prevalence of 1% or higher

**Ag-RDT should have a Sn of 80% and Sp of 97%

Consensus Issues

Despite the very low quality of evidence, the majority voted to strongly recommend the use of both RT-PCR testing and clinical risk assessment to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery primarily due to the potential impact of a false negative result on the safety of the patient and health care staff involved as well as on infection control processes of hospitals. RT-PCR was also recommended as it is now readily available in most hospitals. However, a panelist suggested that RT-PCR and PPE should only be conditionally recommended in areas with prevalence rates of 1% or higher.

The specification of the sensitivity and specificity for the Ag-RDT was the reason for the strong recommendation on the use of clinical risk assessment and Ag-RDT to screen for COVID-19 among asymptomatic individuals scheduled for non-emergency surgery when RT-PCR testing is not available. However, other panelists are concerned if there is an available antigen test that would meet the set specification in terms of sensitivity and specificity.

EVIDENCE SUMMARY

Among asymptomatic individuals scheduled for non-urgent, nonemergency surgery, should RT-PCR and clinical risk assessment vs clinical risk assessment alone be done to screen for COVID-19? Evidence Reviewers: Eva I. Bautista, MD, Patricia Pauline M. Remalante-Rayco, MD, Howell Henrian G. Bayona, MSc

Key Findings

Based on 1 cohort study with very low quality, the diagnostic accuracy of clinical risk assessment alone in detecting COVID-19 compared to RT-PCR was found to be poor, with a sensitivity of 0.42 (95% CI 0.15-0.72) and a specificity of 0.85 (95% CI 0.76-0.92). Clinical risk assessment also results in more false negative and false positive results.



Very low certainty evidence from one economic modeling study suggests that universal preendoscopy virus testing using Ag-RDT, standard RT-PCR, or rapid PCR combined with high risk PPE use in all patients irrespective of test results was more cost-effective compared to no preendoscopy testing and no high risk PPE use, at an assumed prevalence rate of 1% or higher among asymptomatic individuals.

Patients for elective surgery who test positive on any pre-operative COVID-19 tests or clinical assessment were at least 3 times more at risk of experiencing pulmonary complications or death compared to those who test negative based on 1 cohort study with very low quality. Delaying surgery to at least 7 weeks from a COVID-19 diagnosis also showed benefit. Given this data on the risks and benefits associated with a COVID-19 diagnosis as well as the high false negative rates of clinical risk assessment alone, clinical risk assessment would appear to cause more harm compared to more objective tests.

Introduction

The COVID-19 pandemic has led to deferral and postponement of surgeries, especially nonessential or elective ones, in institutions across the globe. Asymptomatic COVID-19 patients undergoing surgery are at a higher risk of postoperative mortality and ICU admission compared to those without COVID-19 [1,2,3]. The proportion of asymptomatic COVID-19 cases is reported to be 17.9% [4]. Hence, ascertaining the COVID-19 status of asymptomatic surgical candidates informs decisions to prevent viral transmission and reduce postoperative complications.

Recommendations for routine RT-PCR testing have been made for elective surgical candidates suspected of COVID-19 based on the availability of the test, turnaround time, availability of PPE and disease prevalence [5]. Its results also depend on sampling technique, specimen handling, and timing of specimen collection from symptom onset [6,7]. False negative rates for RT-PCR were estimated to reach as high as 16% [8].

Clinical risk assessment includes determining history of close contact with a confirmed COVID-19 case (i.e., within 6 feet for a total of 15 minutes or more) and evaluating symptoms. Risk is also considered high if a person has taken part in activities where physical distancing is difficult to maintain such as travel, attending large social or mass gatherings, or being in crowded indoor settings [9]. Its diagnostic performance for screening asymptomatic surgical candidates remains to be determined.

Review Methods

A comprehensive search on PubMed, Cochrane CENTRAL was done with the following search terms using our PICO: COVID-19, SARS-CoV-2, surgery, operation, preoperative, postoperative, testing, RT-PCR. We also searched for preprints on ChinaXiv, MedRxiv and Biorxiv and the reference lists of identified articles. The last search was done on 10 Mar 2021 without language restrictions. We used the following inclusion criteria for this review:

- Study design: randomized controlled trials, controlled clinical trials, observational studies
- Population: asymptomatic individuals scheduled for non-urgent, non-emergency surgery
- Exposure: clinical risk assessment or other pre-operative COVID-19 testing methods
- Outcome: diagnostic accuracy, post-operative outcomes, cost-effectiveness

For the outcome of diagnostic accuracy, we excluded studies that did not report sufficient data to calculate the sensitivity and specificity estimates.



There were no studies that provided direct evidence on the effects of clinical risk assessment and pre-operative RT-PCR testing vs clinical risk assessment alone on management decisions and post-operative outcome in asymptomatic patients scheduled for non-emergency surgery.

Results

Characteristics of included studies

Three eligible studies informed this review [10-12].

One retrospective cohort study assessed the accuracy of clinical risk assessment for screening COVID-19, using RT-PCR as reference standard. In this study, 99 asymptomatic adult patients (mean age 64.1 ± 30 years, scheduled for inpatient orthopedic surgery) underwent both clinical assessment (i.e., temperature testing and Centers for Disease Control and Prevention-based symptom screening questionnaires for COVID-19) and nasopharyngeal swab RT-PCR testing [10].

One multi-center, international, prospective cohort study [11] provided indirect evidence on the impact of pre-operative COVID-19 testing on post-operative outcomes (complications, mortality on day 30). The study involved a total of 140,231 consecutive patients who underwent elective or emergency surgery for any indication. Of these, 3,127 (2.2.%) were confirmed COVID-19 cases (1,384 or 44.3% were asymptomatic, 1,726 or 55.2% were symptomatic, and 17 or 0.5% had unknown symptom status). In this study, COVID-19 diagnosis was made based on either clinical or other objective tests: (a) RT-PCR swab in 79.5% (2486/3127), (b) rapid antigen test in 2.8% (87/3127), (c) CT scan in 3.8% (118/3127), (d) antibody test in 9.0% (280/3127), and (e) a clinical diagnosis in 5.0% (156/3127). However, the study did not report data to allow comparisons between these different types of pre-operative tests on both patients with or without symptoms.

The cost-effectiveness of pre-endoscopy SARS-CoV-2 testing and use of high risk PPE was assessed in one economic evaluation study [12]. The costs, effects, and incremental cost-effectiveness ratios (ICERs) were calculated for 8 different combinations of infection prevention and testing strategies. These testing strategies included clinical signs screening, decentralized point-of-care antigen test, centralized rapid PCR, and standard PCR test. A Monte Carlo simulation for 4 different prevalence rates (0.01%, 0.1%, 1%, and 5%) was done based on a model of 10,000 asymptomatic patients, 20 full-time HCWs wearing two N95 masks per day, and 250 working days.

Methodological quality

Overall quality of the body of evidence was downgraded to very low due to serious risk of bias, indirectness and serious imprecision (Appendix 2). The GRADE rating for retrospective cohort study was low; downgraded due to serious risk of bias and serious imprecision. The GRADE rating for the prospective cohort study was low; downgraded due to indirectness.

Outcomes

Diagnostic accuracy

Clinical risk assessment had a sensitivity of 0.42 (95% Cl 0.15-0.72) and specificity of 0.85 (95% Cl 0.76-0.92) based on 1 retrospective cohort study with very low quality [10]. This translates to a false negative rate of 0.58 and a false positive rate of 0.15.

Harms associated with a false negative



Indirect evidence showing the possible harms resulting from a false negative diagnosis was derived from the prospective cohort study which reported on the post-operative outcomes for patients tested for COVID-19. However, it was not possible to calculate risk ratios specifically for asymptomatic patients or for specific test methods (clinical risk assessment, antigen, RT-PCR). The certainty of this evidence was rated very low due to serious indirectness (combined data from asymptomatic and symptomatic, no subgroup analysis according to testing method).

Among patients who had elective surgery within 0-7 weeks after getting a positive result from any pre-operative COVID-19 test result (not specific to clinical or other testing methods), the risk of 30-day post-operative mortality and pulmonary complications were both at least 3 times higher (RR 3.96 (95% CI 3.41, 4.59) and (RR 3.41, 95% CI 3.04,3.83) compared to those who tested negative [11].

Surgeries that were delayed after ascertainment of the patients' COVID-19 status showed better post-surgical outcomes--however, this effect was only significant for surgeries done at least 7 weeks from COVID-19 diagnosis. In particular, post-operative mortality and complications were comparable to patients without COVID-19, with an RR of 1.46 (95% CI 0.73 - 2.92) and 1.37 (95% CI 0.91 - 2.08), respectively [11].

Cost-effectiveness

Very low certainty evidence suggests that universal pre-endoscopy virus testing using Ag-RDT, standard RT-PCR, or rapid PCR combined with high-risk PPE use in all patients irrespective of test results was found to be more cost-effective compared to no pre-endoscopy testing and no high risk PPE use, at an assumed prevalence rate of 1% or higher among asymptomatic individuals. Among the different tests, Ag-RDT with high-risk PPE was found to be the most cost-effective strategy (ICER = -26,286 €) followed by rapid PCR with high risk PPE use (ICER = -13,703 €) then standard RT-PCR (ICE= -11,128€). The high cost of standard PCR (273.35€) and rapid PCR (167.85€) compared with rapid Ag test (17.30€) as well as their turnaround times (standard PCR=2 days, Rapid PCR=1 day, Ag-RDT<1 day) seemed to favor Ag-RDT in terms of cost-effectiveness [13]. The quality for this evidence was very low due to very serious risk of bias (use of assumptions/simulations versus observational data, incomplete costing data) and serious indirectness (different country, healthcare system).

Recommendations from Other Groups

Both CDC (07 December 2020) and IDSA (23 December 2020) **suggest RT-PCR testing** of asymptomatic individuals without known exposure when the results will impact isolation/quarantine/personal protective equipment (PPE) usage decisions, dictate eligibility for surgery [9,13].

Similarly, IDSA **suggests RT-PCR** testing for asymptomatic individuals without known exposure to COVID-19 who are undergoing major time-sensitive surgeries (i.e., medically necessary surgeries that need to be done within 3 months). To limit potential poor outcomes, deferring nonemergent surgeries should be considered for patients testing positive for SARS-CoV-2. Decisions about PPE use for the aerosol generating portions of these procedures may be dependent on test results when PPE supplies are limited. However, due to the risk of false negatives, caution should be exercised by healthcare workers who will be in close contact with/exposed to the upper respiratory tract (e.g., anesthesia personnel, ENT procedures).

The Philippine Society for Microbiological and Infectious Diseases (PSMID) and Philippine Hospital Infection Control Society (PHICS) (26 May 2020) **recommend COVID-19 clinical risk**



assessment for patients about to undergo surgery, **and if available, RT-PCR**. Accessibility, turnaround time, and cost-effectiveness (cost of RT-PCR vs. cost of PPE) are important considerations when RT-PCR is to be requested. [5]

On the other hand, PSMID, and PHICS **recommend RT-PCR** particularly for individuals who will undergo high-risk surgical procedures, even if they are asymptomatic [5]. Other national and international groups **recommend preoperative RT-PCR testing**, some regardless of symptoms or exposure [14-18]

Research Gaps

Currently, there are no ongoing studies on this topic.

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Author	Study Design	Patient Selection	Outcome
Gruskay	Retrospective	n=99	Sensitivity
2020	cohort	Symptomatic and asymptomatic patients who had preoperative RT-PCR testing prior to orthopedic surgery	Specificity
COVIDSrug Collaborative 2021	International, prospective cohort	n=96,018 Symptomatic and asymptomatic RT- PCR-confirmed COVID-19	Post-operative complications and 30-day post-operative mortality within 0-2 weeks after COVID-19 diagnosis
		Patients without COVID-19 diagnosis	Post-operative complications 30-day post-operative mortality if elective surgery was delayed from at least 7 weeks after COVID-19 diagnosis

Appendix 1. Characteristics of Included Studies



Author	Study Design	Patient Selection	Outcome
Ebigbo 2020 Germany	Model- based assumption	10 000 asymptomatic patients scheduled for endoscopy	Incremental Cost-effectiveness Ratio

Appendix 2. GRADE Evidence Profile

Sensitivity	0.42 (95% CI: 0.19 to 0.68)
Specificity	0.85 (95% CI: 0.76 to 0.91)

Outcome	Nº of studies	Study design	Fact	ors that may	y decrease ce	ertainty of e	vidence	Effect per 1,000 patients tested			Test accuracy
	patient s)		Risk of bias	Indirectn ess	Inconsiste ncy	Imprecis ion	Publicat ion bias	pre-test probabi lity of 5%	pre-test probabi lity of 24%	pre-test probabi lity of 32%	COE
True positives (patients with COVID-19)	1 studies 12 patient s	cross- sectional (cohort type accuracy	serio us _{1,a,b}	not serious	not serious	serious _{1,c}	none	21 (10 to 34)	101 (46 to 163)	134 (61 to 218)	⊕⊕⊖ ⊖ Low
False negatives (patients incorrectly classified as not having COVID-19)		study)						29 (16 to 40)	139 (77 to 194)	186 (102 to 259)	
True negatives (patients without COVID-19)	1 studies 87 patient s	cross- sectional (cohort type accuracy study)	serio US ^{1,a,b}	not serious	not serious	not serious 1,c	none	808 (722 to 864)	646 (578 to 692)	578 (517 to 619)	⊕⊕⊕ ○ MODER ATE
False positives (patients incorrectly classified as having COVID-19)								142 (86 to 228)	114 (68 to 182)	102 (61 to 163)	

Explanations

a. The interval between clinical risk assessment and RT-PCR testing was not reported.b. The study excluded 42 patients (30% of the recruited participants) who had clinical risk assessment but no RT-PCR testing.

c. The sample size was small (n=99).

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			Certainty ass	sessment			№ of patients		Effect		Certainty	Importance
N⁰ of studi es	Study design	Risk of bias	Inconsiste ncy	Indirectn ess	Imprecisi on	Other considerations	COVID- 19 patients	non- COVID-19 patients	Relative (95% Cl)	Absolute (95% Cl)		

Postoperative 30-day mortality

1	observatio nal studies	not serious	not serious	very serious 1,a,b	not serious	none	17/338 (5.0%)	588/9568 0 (0.6%)	RR 8.18 (5.11 to 13.10)	44 more per 1,000 (from 25 more to 74 more)	

Pulmonary complications

1	observatio nal studies	not serious	not serious	very serious _{1,a,b}	not serious	none	21/338 (6.2%)	1720/956 80 (1.8%)	RR 3.46 (2.28 to 5.24)	44 more per 1,000 (from 23 more to 76 more)	
										more)	

Post-operative mortality (Surgery delayed for at least 7 weeks after COVID-19 diagnosis)

1	observatio nal studies	not serious	not serious	very serious _{1,a,b}	not serious	none	8/892 (0.9%)	588/9568 0 (0.6%)	RR 1.46 (0.73 to 2.92)	3 more per 1,000 (from 2 fewer to 12 more)	
1											1

Post-operative complications (Surgery delayed for at least 7 weeks after COVID-19 diagnosis)

1	observatio nal studies	not serious	not serious	very serious 1,a,b	not serious	none	22/892 (2.5%)	1720/956 80 (1.8%)	RR 1.37 (0.91 to 2.08)	7 more per 1,000 (from 2 fewer to 19 more)	

Cl: Confidence interval; RR: Risk ratio

Explanations

a. The study compared the outcomes of surgery between those with COVID-19 or no COVID-19 based on PCR testing, rather than outcomes of surgery based on clinical risk assessment alone vs clinical risk assessment and PCR testing

b. There was indirectness that was attributed to combined symptomatic (55.2%) and asymptomatic (44.8%) COVID-19 patients.

References

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Appendix 3. Forest Plot

Study	ΤР	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Gruskay 2020	5	13	7	74	0.42 [0.15, 0.72]	0.85 [0.76, 0.92]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

Figure 1. Forest plot of the sensitivity and specificity of clinical risk assessment in diagnosing COVID-19.

Г		COVID	-19	No COV	/ID-19		Risk Ratio		Risk Ratio
5	study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M–H, Fixed, 95% CI
ſ	COVIDSurg 2021	178	3127	1973	137104	100.0%	3.96 [3.41, 4.59]		
1	Fotal (95% CI)		3127		137104	100.0%	3.96 [3.41, 4.59]		•
1	lotal events	178		1973					
۱,	leterogeneity: Not app	plicable						0.001	0 1 1 10 1000
ין	lest for overall effect:	Z = 18.0)6 (P <	0.00001)			0.001	Favours [COVID-19] Favours [No COVID-19]

Figure 2. Forest Plot of Post-operative mortality

	COVID	-19	No COV	ID-19		Risk Ratio		Risk	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% CI
23.1.1 Elective Surge	ry								
COVIDSurg 2021	47	1762	588	95680	19.4%	4.34 [3.24, 5.82]			+
Subtotal (95% CI)		1762		95680	19.4%	4.34 [3.24, 5.82]			•
Total events	47		588						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 9.81	(P < 0	.00001}						
23.1.2 Emergency Su	rgery								
COVIDSurg 2021	131	1365	1385	41413	80.6X	2.87 [2.42, 3.40]			
Subtotal (95% CI)		1365		41413	80.6%	2.87 [2.42, 3.40]			•
Total events	131		1385						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 12.0	9 (P <	0.00001)	•					
Total (95% CI)		3127		137093	100.0%	3.15 [2.72, 3.66]			•
Total events	178		1973						
Heterogeneity: Chi ² =	5.73, df	- 1 (P	= 0.02); 1	² = 83×			0.002	01	10 500
Test for overall effect:	Z = 15.2	9 (P <	0.00001)	•			0.002 Fi	VOURS (COVID-19)	Favours [No COVID-19]
Test for subgroup diff	erences: (Chi ² - !	5.71, df -	1 (P = 0	.02), P =	82.5%	14	10013 [00410-13]	1410013 [110 COVID-13]

Figure 3. Forest Plot of Post-operative mortality (urgency of surgery)

	COVID-19		No COVID-19		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	ed, 95% CI
COVIDSurg 2021	284	3127	3654	137093	100.0%	3.41 [3.04, 3.82]			
Total (95% CI)		3127		137093	100.0%	3.41 [3.04, 3.82]			•
Total events	284		3654						
Heterogeneity: Not applicable Test for overall effect: Z = 20.82 (P < 0.00001)						0.01	0.1 Favours [COVID-19]	1 10 100 Favours [No COVID-19]	





	COVID	-19	No COV	ID-19		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
22.1.1 Elective Surgery							
COVIDSurg 2021	104	1762	1720	95680	33.5X	3.28 [2.71, 3.98]	•
Subtotal (95% CI)		1762		95680	33.5%	3.28 [2.71, 3.98]	•
Total events	104		1720				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 12.1	2 (P <	0.00001)	•			
22.1.2 Emergency Su	22.1.2 Emergency Surgery						
COVIDSurg 2021	180	1365	1934	41413	66.5X	2.82 [2.45, 3.26]	
Subtotal (95% CI)		1365		41413	66.5%	2.82 [2.45, 3.26]	•
Total events	180		1934				
Heterogeneity: Not ap	plicable						
Test for overall effect: $Z = 14.24 (P < 0.00001)$							
		-					
Total (95% CI)		3127		137093	100.0%	2.98 [2.66, 3.34]	•
Total events	284		3654				
Heterogeneity: $Chi^2 = 1.52$, $df = 1$ (P = 0.22); $l^2 = 34\%$							
Test for overall effect: $Z = 18.66 (P < 0.00001)$							
Test for subgroup differences: Ch ² = 1.52, df = 1 (P = 0.22), l ² = 34.3%							

Figure 5. Forest Plot of Post-operative pulmonary complications (urgency of surgery)

Appendix 4. Cost Effectiveness of Pre-endoscopy testing and use of highrisk PPE (Emigmo, 2020)

Strategy		ICER value					
		Prevalence					
		0.01% (0.005-0.02)	1% (0.5-2%)	5% (2.5-10%)			
		€	€	€			
Control Strategy:							
No c	diagnostic test						
No	high risk PPE						
	no high risk PPE	11,774	-13,035	-15,240			
Ag test	high risk PPE	17,451	-22,716	-26,286			
	no high risk PPE	145,570	345	-12, 564			
Rapid PCR	high risk PPE	155, 150	659	-13,073			
	no high risk PPE	249,022	10,690	-10,495			
Standard PCR	high risk PPE	258,557	10,887	-11, 128			

Appendix 5. Sensitivity and specificity of the tests (Emigmo, 2020)

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	Standard PCR Cobas	Rapid PCR	Rapid Antigen test
	Assay	Xpert Cepheid	
Sensitivity (95% CI)	0.97 (0.92-0.97)	0.95 (0.92-0.98)	0.57 (0.48-0.6)
Specificity (95% CI)	1.00 (0.96- 0.99)	1.00 (0.96-0.99)	1.00 (0.98-0.99)

Appendix 6. Cost and turn-around time of SARS-CoV2 virus tests (Emigmo, 2020)

	Standard PCR test	Rapid PCR test	Rapid Ag test
Cost (€)	273.35	167.85	17.30
Turnaround time	48	24	
(hours)			